But wait, there are more myeloid white blood cells. The next series show cells that not only phagocytize, they also process proteins from the pathogen and place them on other proteins, MHC proteins, that exhibit them to Th cells. These are the professional antigen presenting cells and metaphorically, they represent the cavalry and the scouts that report in to the army officers. Here is a picture of a monocyte. These two monocytes are actually immature forms, they're going to usually grow up to be macrophages. Here is a rendering of a monocyte and so when this monocyte continues to mature, it will enlarge five to ten times and it will, again, begin to make a lot of inclusions and other molecules that will be important in hydrolyzing pathogens, breaking them up and using them to alert Th cells. So, in this picture, we have one of the mature versions of this and this is a really cool unusual one of a macrophage. Usually, you don't have two different huge extensions from it, but it is just a reminder that these guys not only phagocytize but they're going to reach out and attempt to transmit information, or they may be reaching out and trying to grab pathogens. But the picture of the cell as being some little blob with round on the outside really doesn't do these guys or the next guys any justice whatsoever, they have very active surfaces and they move around a lot and they extend parts of themselves out to phagocytize things, so they are strongly phagocytic. So, we have chosen to represent this one as a phagocytic cell about to grab some hapless pathogen. Also, we put it on a horselike structure because these are like the cavalry, that is they don't just sit there, they grab things and then they go looking for Th cells to alert. So, again they protect you by killing things phagocytically and they also transmit information and the cavalry is a good analogy, at least as good as one that I can come up with. Now, we have a light microscope picture of a dendritic cell. They're called dendritic because, like your nerve cells with their dendrites, they have lots of extensions of their plasma membranes. But in fact, of course, they're not nerve cells that all, they're immune cells. Now, these guys come in a bunch of different subtypes and I collectively refer to them as sentinel dendritic cells because they function as scouts or patrols of the immune system. This term, this metaphor also emphasizes that these cells are the first to present an antigen to naive Th cells, and are the major gatekeepers of the system deciding whether or not a Th cell will respond to a new antigen. That is, these are going to be the very first cells that are capable of alerting your adaptive immune system to a new pathogenic threat. Now, this is an artist's rendering of a dendritic cell from Subramanian and Donald Bliss and you can see that this is a completely different way of looking at a dendritic cell. This one looks to me a lot like a flower, and it's very beautiful. It represents the cell morphology when the dendritic cell is not actively migrating but rather lying in wait in a tissue, waiting to phagocytize antigen, digest it and then present it to a Th cell. Now, next to this is a light micrograph of a dendritic cell that is, as we can see, on the move. It has picked up some antigen and is presenting it, and is now wandering around looking for a Th cell to present it to. This is from one of my former Immuno students, Allison Skinkle. So, it shows the morphology of a sentinel dendritic cell as it moves to find a Th cell to present to. So, to make sense of what the dendritic cells do because they really have these quite complex functions, we have one of our cartoons from Daisy Chung and so here is her representation of a sentinel dendritic cell as being one of the scouts of the immune system and she decided to show this as a Girl Scout. We'll return to the functional details shown here but for now, I'm just going to show you that she is sticking out a hand with some MHC holding- is that a fly? Flies are terrible for containing diseases and spreading them around. The fly represents, of course, the antigen that she's presenting to a Th cell. Let's see, you can also see that she has a badge reminding you that she's the number one first antigen presenter and she has a bunch of signaling molecule shown as Girl Scout Cookies at her feet, so these are also important in doing chemical signaling. So, a final factoid, some sentinel dendritic cells are actually part of the lymphoid lineage, not just the myeloid lineage and so it's a very interesting and complex category of cells. Now, my personal suspicion is we're going to learn more about this and give you a better picture of how the cells differentiate and perform to both alert the immune system and upregulate it and also to downregulate it when the antigen does not represent a threat. Finally, here is a follicular dendritic cell. Now, this cell is important to improving immune function, but in all other ways it's

a cell type totally different from all those other immune cells. Note that this has an incredible number of extensions, again the reason for the word dendritic in the name. So, although you don't see them on this particular cell, these extensions can trap particles and antigen antibody complexes called exosomes, and these exosomes appear in our cartoon. So, here's our cartoon of the follicular dendritic cell and you can see that it's supporting happy B-cell development and those little yellow dots are the exosomes. These are the little representations of complexes of antigen and antibody and you can see that some of our little B-cells are binding to this very well and that means they have really good receptors and they're going to get the signals that make them grow and divide. Sadly, the ones that don't do that are not pictured here because they're undergoing apoptosis. So, we have our follicular dendritic cell instructing B-cells and it's instructing them by giving them a chance to bind to a particular antigen antibody complex and thus get some encouragement in their development. Now, just to wrap it up, we saw a number of examples of dendritic cells and they were all really very different. We had nerve cells that had dendrites or extension sticking out from them, nerve cells really don't play a huge direct role in the immune response, but they do determine how much energy you want to put into it. Sentinel dendritic cells are very important in the immune system. Even though they are myeloid and not part of the lymphoid system, they're very important in alerting lymphoid cells and upregulating the adaptive immune system. Finally, we have the follicular dendritic cells which are quite unusual in that they don't arise from haematopoiesis and yet still, they are very important in determining how B-cells develop. Again, all three of these cell types have in common that they have dendritic or very hairy extensions and not much else.